



BILLING CODE 6560-50-P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2018-0677; FRL-9993-11]

Pyriofenone; Pesticide Tolerances

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes tolerances for residues of pyriofenone in or on fruiting vegetable, crop group 8-10. ISK Biosciences Corporation requested these tolerances under the Federal Food, Drug, and Cosmetic Act (FFDCA).

DATES: This regulation is effective *[insert date of publication in the Federal Register]*.

Objections and requests for hearings must be received on or before *[insert date 60 days after date of publication in the Federal Register]* and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA-HQ-OPP-2018-0677, is available at <http://www.regulations.gov> or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), West William Jefferson Clinton Bldg., Rm. 3334, 1301 Constitution Ave., NW., Washington, DC 20460-0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566-1744, and the telephone number for the OPP Docket is (703)

305-5805. Please review the visitor instructions and additional information about the docket available at <http://www.epa.gov/dockets>.

FOR FURTHER INFORMATION CONTACT: Michael Goodis, Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; main telephone number: (703) 305-7090; email address: RDfRNotices@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. How Can I Get Electronic Access to Other Related Information?

You may access a frequently updated electronic version of EPA's tolerance regulations at 40 CFR part 180 through the Government Publishing Office's e-CFR site at http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl.

C. How Can I File an Objection or Hearing Request?

Under FFDCA section 408(g), 21 U.S.C. 346a, any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA-HQ-OPP-2018-0677 in the subject line on the first page of your submission. All objections and requests for a hearing must be in writing, and must be received by the Hearing Clerk on or before *[insert date 60 days after date of publication in the **Federal Register**]*. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI)) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request, identified by docket ID number EPA-HQ-OPP-2018-0677, by one of the following methods:

- *Federal eRulemaking Portal*: <http://www.regulations.gov>. Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be CBI or other information whose disclosure is restricted by statute.

- *Mail*: OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.

- *Hand Delivery*: To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at <http://www.epa.gov/dockets/contacts.html>.

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at <http://www.epa.gov/dockets>.

II. Summary of Petitioned-For Tolerance

In the **Federal Register** of December 21, 2018 (83 FR 65660) (FRL-9985-67), EPA issued a document pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide petition (PP 7F8647) by ISK Biosciences Corporation, 7470 Auburn Road, Suite A, Concord, Ohio 44077. The petition requested that 40 CFR 180.660 be amended by establishing tolerances for residues of the fungicide pyriofenone, in or on fruiting vegetable, crop group 8-10 at 0.30 parts per million (ppm). That document referenced a summary of the petition prepared by ISK Biosciences Corporation, the registrant, which is available in the docket, <http://www.regulations.gov>. There were no comments received in response to the notice of filing. Based upon review of the data supporting the petition and under its authority in FFDCA section 408(d)(4)(A)(i), EPA is establishing a tolerance that varies slightly from what the petitioner sought. The reason for this change is explained in Unit IV.C.

III. Aggregate Risk Assessment and Determination of Safety

Section 408(b)(2)(A)(i) of FFDCA allows EPA to establish a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the tolerance is “safe.” Section 408(b)(2)(A)(ii) of FFDCA defines “safe” to mean that “there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.” This includes exposure through drinking water and in residential settings, but does not include occupational exposure. Section 408(b)(2)(C) of FFDCA requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to “ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue....”

Consistent with FFDCA section 408(b)(2)(D), and the factors specified in FFDCA section 408(b)(2)(D), EPA has reviewed the available scientific data and other relevant information in support of this action. EPA has sufficient data to assess the hazards of and to make a determination on aggregate exposure for pyriofenone including exposure resulting from the tolerances established by this action. EPA's assessment of exposures and risks associated with pyriofenone follows.

A. Toxicological Profile

EPA has evaluated the available toxicity data and considered its validity, completeness, and reliability as well as the relationship of the results of the studies to human risk. EPA has also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children.

The liver (dog, rat, and mouse), kidney (rat and mouse), and cecum (rat) were the primary organs affected in toxicity studies associated with the species identified above. Indications of liver toxicity included increased weight, dark color, histological abnormalities, and serum hepatic enzyme changes. Indications of kidney toxicity included increased weight, coarse surface, histological abnormalities, increased urinary ketones, and perigenital staining. Cecum effects included increased weight; and enlarged, distended, and inflamed conditions. There are no inhalation risks of concern, due to high margins of exposure via the inhalation route as well as very low toxicity observed in the acute inhalation toxicity study (Toxicity Category IV). Based on a weight of evidence approach, it was determined that a subchronic inhalation study was not required. No dermal toxicity was noted at the limit dose. No developmental toxicity was noted at the limit dose in rats; abortions were noted in rabbits at 300 mg/kg/day. The rabbit abortions were associated with decreased maternal body weight gain and food consumption. There was no

reproductive toxicity observed at the highest dose tested in rats (334 mg/kg/day), no neurotoxicity observed in the database, and no quantitative or qualitative sensitivity was noted in offspring. Based on a battery of mutagenicity studies, there was no evidence of genotoxicity nor an increased incidence of tumors. There was no evidence that pyriofenone directly targets the immune system based on the results of the immunotoxicity study and the other studies in the toxicity database. Based on a lack of evidence of carcinogenicity in available studies conducted with mice and rats, pyriofenone is classified as “Not Likely to Be Carcinogenic to Humans.”

Specific information on the studies received and the nature of the adverse effects caused by pyriofenone as well as the no-observed-adverse-effect-level (NOAEL) and the lowest-observed-adverse-effect-level (LOAEL) from the toxicity studies can be found at <http://www.regulations.gov> in document ***Pyriofenone. Human Health Risk Assessment for the Section 3 Registration on Fruiting Vegetables (Crop Group 8-10)*** on pages 29-37 in docket ID number EPA-HQ-OPP-2018-0677.

B. Toxicological Points of Departure/Levels of Concern

Once a pesticide’s toxicological profile is determined, EPA identifies toxicological points of departure (POD) and levels of concern to use in evaluating the risk posed by human exposure to the pesticide. For hazards that have a threshold below which there is no appreciable risk, the toxicological POD is used as the basis for derivation of reference values for risk assessment. PODs are developed based on a careful analysis of the doses in each toxicological study to determine the dose at which no adverse effects are observed (the NOAEL) and the lowest dose at which adverse effects of concern are identified (the LOAEL). Uncertainty/safety factors are used in conjunction with the POD to calculate a safe exposure level - generally referred to as a population-adjusted dose (PAD) or a reference dose (RfD) - and a safe margin of exposure

(MOE). For non-threshold risks, the Agency assumes that any amount of exposure will lead to some degree of risk. Thus, the Agency estimates risk in terms of the probability of an occurrence of the adverse effect expected in a lifetime. For more information on the general principles EPA uses in risk characterization and a complete description of the risk assessment process, see <http://www.epa.gov/pesticides/factsheets/riskassess.htm>.

A summary of the toxicological endpoints for pyriofenone used for human risk assessment is shown in Table 1 of this unit.

Table --Summary of Toxicological Doses and Endpoints for Pyriofenone for Use in Human Health Risk Assessment

Exposure/Scenario	Point of Departure and Uncertainty/Safety Factors	RfD, PAD, LOC for Risk Assessment	Study and Toxicological Effects
Acute dietary (All populations)	A dose and endpoint of concern attributable to a single dose was not observed.		
Chronic dietary (All populations)	NOAEL= 9.1 mg/kg/day UF _A = 10x UF _H = 10x FQPA SF = 1x	Chronic RfD = cPAD = 0.091 mg/kg/day	Carcinogenicity in rat LOAEL = 46.5 mg/kg/day based on chronic nephropathy in females
Cancer (Oral, dermal, inhalation)	Classification: "Not likely to be Carcinogenic to Humans"		

FQPA SF = Food Quality Protection Act Safety Factor. LOAEL = lowest-observed-adverse-effect-level. LOC = level of concern. mg/kg/day = milligram/kilogram/day. MOE = margin of exposure. NOAEL = no-observed-adverse-effect-level. PAD = population adjusted dose (a = acute, c = chronic). RfD = reference dose. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies).

C. Exposure Assessment

1. *Dietary exposure from food and feed uses.* In evaluating dietary exposure to pyriofenone, EPA considered exposure under the petitioned-for tolerances as well as all existing pyriofenone tolerances in 40 CFR 180.660. EPA assessed dietary exposures from pyriofenone in food as follows:

i. *Acute exposure.* Quantitative acute dietary exposure and risk assessments are performed for a food-use pesticide, if a toxicological study has indicated the possibility of an effect of concern occurring as a result of a 1-day or single exposure. No such effects were identified in the toxicological studies for pyriofenone; therefore, a quantitative acute dietary exposure assessment is unnecessary.

ii. *Chronic exposure.* In estimating chronic dietary exposure, EPA used food consumption information from the United States Department of Agriculture's National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/WWEIA) as incorporated in the Dietary Exposure and Evaluation Model with Food Commodity Intake Database (DEEM-FCID) Version 3.16. As to residue levels in food, EPA assumed 100 percent crop treated (PCT) and tolerance-level residues. Potential residues in drinking water were included in the DEEM-FCID categories "water, all sources" and "water, indirect all sources". All populations were evaluated for chronic dietary exposure and risk from food and drinking water.

iii. *Cancer.* Based on the data summarized in Unit III.A., EPA has concluded that pyriofenone is not likely to be carcinogenic; therefore, a dietary exposure assessment for the purpose of assessing cancer risk is unnecessary.

iv. *Anticipated residue and percent crop treated (PCT) information.* EPA did not use anticipated residue and/or PCT information in the dietary assessment for pyriofenone. Tolerance level residues and 100 PCT were assumed for all food commodities.

2. *Dietary exposure from drinking water.* The Agency used screening-level water exposure models in the dietary exposure analysis and risk assessment for pyriofenone in drinking water. These simulation models take into account data on the physical, chemical, and fate/transport characteristics of pyriofenone. Further information regarding EPA drinking water

models used in pesticide exposure assessment can be found at

<http://www.epa.gov/oppefed1/models/water/index.htm>.

Based on the Tier I Cranberry Model and Pesticide Root Zone Model Ground Water (PRZM GW), the estimated drinking water concentrations (EDWCs) of pyriofenone for chronic exposures for non-cancer assessments are estimated to be 2.7 ppb for surface water and 3.9 ppb for ground water.

Modeled estimates of drinking water concentrations were directly entered into the dietary exposure model. For chronic dietary risk assessment, the water concentration value of 3.9 ppb was used to assess the contribution to drinking water.

3. *From non-dietary exposure.* The term “residential exposure” is used in this document to refer to non-occupational, non-dietary exposure (e.g., for lawn and garden pest control, indoor pest control, termiticides, and flea and tick control on pets). Pyriofenone is not registered for any specific use patterns that would result in residential exposure. Therefore, a residential exposure assessment is not required.

4. *Cumulative effects from substances with a common mechanism of toxicity.* Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, the Agency consider “available information” concerning the cumulative effects of a particular pesticide's residues and “other substances that have a common mechanism of toxicity.” EPA has not found pyriofenone to share a common mechanism of toxicity with any other substances, and pyriofenone does not appear to produce a toxic metabolite produced by other substances. For the purposes of this tolerance action, therefore, EPA has assumed that pyriofenone does not have a common mechanism of toxicity with other substances. For information regarding EPA's efforts to determine which chemicals have a common mechanism

of toxicity and to evaluate the cumulative effects of such chemicals, see EPA's website at <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/cumulative-assessment-risk-pesticides>.

D. Safety Factor for Infants and Children

1. *In general.* Section 408(b)(2)(C) of FFDCA provides that EPA shall apply an additional tenfold (10X) margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure unless EPA determines based on reliable data that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the FQPA Safety Factor (SF). In applying this provision, EPA either retains the default value of 10X, or uses a different additional safety factor when reliable data available to EPA support the choice of a different factor.

2. *Prenatal and postnatal sensitivity.* Exposure to pyriofenone did not result in any developmental effects at the limit dose in rats, but abortions were noted in rabbits at 300 mg/kg/day. EPA is regulating pyriofenone at doses that are protective of this effect. The abortions were associated with decreased maternal body weight gain and food consumption. There were no reproductive effects observed in rats at the highest tested dose (334 mg/kg/day), nor was any quantitative or qualitative sensitivity noted in offspring.

3. *Conclusion.* EPA has determined that reliable data show the safety of infants and children would be adequately protected if the FQPA SF were reduced to 1X. That decision is based on the following findings:

- i. The toxicity database for pyriofenone is complete.

ii. There is no indication that pyriofenone is a neurotoxic chemical and there is no need for a developmental neurotoxicity study or additional uncertainty factors (UFs) to account for neurotoxicity.

iii. There is no evidence that pyriofenone results in increased susceptibility in *in utero* rats or rabbits in the prenatal developmental studies or in young rats in the 2-generation reproduction study.

iv. There are no residual uncertainties identified in the exposure databases. The chronic dietary food exposure assessment was performed based on 100 PCT and tolerance-level residues. EPA made conservative (protective) assumptions in the ground and surface water modeling used to assess exposure to pyriofenone in drinking water. These assessments will not underestimate the exposure and risks posed by pyriofenone.

E. Aggregate Risks and Determination of Safety

EPA determines whether acute and chronic dietary pesticide exposures are safe by comparing aggregate exposure estimates to the acute PAD (aPAD) and chronic PAD (cPAD). For linear cancer risks, EPA calculates the lifetime probability of acquiring cancer given the estimated aggregate exposure. Short-, intermediate-, and chronic-term risks are evaluated by comparing the estimated aggregate food, water, and residential exposure to the appropriate PODs to ensure that an adequate MOE exists.

1. *Acute risk.* An acute aggregate risk assessment takes into account acute exposure estimates from dietary consumption of food and drinking water. No adverse effect resulting from a single oral exposure was identified and no acute dietary endpoint was selected. Therefore, pyriofenone is not expected to pose an acute risk.

2. *Chronic risk.* Using the exposure assumptions described in this unit for chronic exposure, EPA has concluded that chronic exposure to pyriofenone from food and water will utilize 6.9% of the cPAD for children 1-2 years old the population group receiving the greatest exposure. There are no residential uses for pyriofenone, therefore, the chronic aggregate risk is limited to the chronic dietary risk and is not of concern.

3. *Short-term risk.* Short-term aggregate exposure takes into account short-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level). There are no residential uses for pyriofenone; therefore, short-term aggregate risks are addressed by the chronic aggregate risk estimates and are not of concern.

4. *Intermediate-term risk.* Intermediate-term aggregate exposure takes into account intermediate-term residential exposure plus chronic exposure to food and water (considered to be a background exposure level). There are no residential uses for pyriofenone; therefore, intermediate-term aggregate risks are addressed by the chronic aggregate risk estimates and are not of concern.

5. *Aggregate cancer risk for U.S. population.* Based on the lack of evidence of carcinogenicity in two adequate rodent carcinogenicity studies, pyriofenone is not expected to pose a cancer risk to humans.

6. *Determination of safety.* Based on these risk assessments, EPA concludes that there is a reasonable certainty that no harm will result to the general population, or to infants and children from aggregate exposure to pyriofenone residues.

IV. Other Considerations

A. Analytical Enforcement Methodology

Adequate enforcement methodology (liquid chromatography method with tandem mass spectrometric detection [LC-MS/MS]) is available to enforce the tolerance expression. The method was independently validated to a limit of quantitation (LOQ) of 0.01 ppm in grapes, wheat grain, and wheat straw.

B. International Residue Limits

In making its tolerance decisions, EPA seeks to harmonize U.S. tolerances with international standards whenever possible, consistent with U.S. food safety standards and agricultural practices. EPA considers the international maximum residue limits (MRLs) established by the Codex Alimentarius Commission (Codex), as required by FFDCA section 408(b)(4). The Codex Alimentarius is a joint United Nations Food and Agriculture Organization/World Health Organization food standards program, and it is recognized as an international food safety standards-setting organization in trade agreements to which the United States is a party. EPA may establish a tolerance that is different from a Codex MRL; however, FFDCA section 408(b)(4) requires that EPA explain the reasons for departing from the Codex level. The Codex has not established a MRL for pyriofenone.

C. Revisions to Petitioned-For Tolerances

Under FFDCA section 408(d)(4)(A)(i), EPA may establish tolerances that vary from those sought by the petition. EPA has modified the commodity definition to be consistent with Agency nomenclature. Additionally, the tolerance level has been modified to be consistent with the Agency's rounding class practice.

V. Conclusion

Therefore, tolerances are established for residues of pyriofenone, including its metabolites and degradates in or on fruiting vegetable, crop group 8-10 at 0.3 ppm.

VI. Statutory and Executive Order Reviews

This action establishes tolerances under FFDCA section 408(d) in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled “Regulatory Planning and Review” (58 FR 51735, October 4, 1993). Because this action has been exempted from review under Executive Order 12866, this action is not subject to Executive Order 13211, entitled “Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use” (66 FR 28355, May 22, 2001) or Executive Order 13045, entitled “Protection of Children from Environmental Health Risks and Safety Risks” (62 FR 19885, April 23, 1997), nor is it a regulatory action under Executive Order 13771, entitled “Reducing Regulations and Controlling Regulatory Costs” (82 FR 9339, February 3, 2017). This action does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA) (44 U.S.C. 3501 *et seq.*), nor does it require any special considerations under Executive Order 12898, entitled “Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations” (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerance in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 *et seq.*), do not apply.

This action directly regulates growers, food processors, food handlers, and food retailers, not States or tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCA section 408(n)(4). As such, the Agency has determined that this action will not have a substantial direct

effect on States or tribal governments, on the relationship between the national government and the States or tribal governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian tribes. Thus, the Agency has determined that Executive Order 13132, entitled “Federalism” (64 FR 43255, August 10, 1999) and Executive Order 13175, entitled “Consultation and Coordination with Indian Tribal Governments” (65 FR 67249, November 9, 2000) do not apply to this action. In addition, this action does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act (UMRA) (2 U.S.C. 1501 *et seq.*).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act (NTTAA) (15 U.S.C. 272 note).

VII. Congressional Review Act

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq.*), EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This action is not a “major rule” as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: May 22, 2019.

Michael Goodis,

Director, Registration Division, Office of Pesticide Programs.

Therefore, 40 CFR chapter I is amended as follows:

PART 180--[AMENDED]

1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

2. In § 180.660, add alphabetically “Vegetable, fruiting, group 8-10” to the table in paragraph (a) to read as follows:

§ 180.660 Pyriofenone; tolerances for residues.

(a) * * *

Commodity	Parts per million
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Vegetable, fruiting, group 8-10	0.3
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[FR Doc. 2019-11261 Filed: 5/29/2019 8:45 am; Publication Date: 5/30/2019]